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EXAMINER	
MARVICH, MARIA	
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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/072,766	SLEPIAN, MARVIN J.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6-13,15-33 and 35-37* is/are pending in the application.

4a) Of the above claim(s) *8-12,26,27 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,7,13,15-25,28-33 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 6-13, 15-33 and 35-38 are pending in the instant application. Claims 8-12, 26, 27 and 30 have been withdrawn. Hence, claims 1, 3, 6, 7, 13, 15-25, 28-33 and 35-37 are under examination.

Claim Objections

Claims 18 and 19 are objected to because of the following informalities: claim 18 refers to "a therapeutic, prophylactic or diagnostic agent" in claim 15. It is customary when referring to limitations to reference them using the article "the" as opposed to "a" for clarity. Similarly, in claim 19, the recitation "a void, cavity, containment space or reservoir" is referring to limitations previously recited in claim 15. For clarity, it would be remedial to amend the article "a" in each of these cases to --the--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6-7, 13 and 15-24 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. **This rejection is maintained for reasons of record in the office action mailed 9/7/05 and restated below.**

Claim 1 has been amended to recite, "wherein the agent is in a polymeric carrier for local delivery of an effective amount of the therapeutic, prophylactic or diagnostic agent". As well that the "polymeric carrier is selected from the group consisting of porous matrices, hydrogels, organogels, colloidal suspensions, microparticles and microcapsules, nanoparticles and combinations thereof" has been added to claims 1 and 15. Applicants have indicated that support for this limitation is found in original claim 5, page 8, lines 16-30, page 12, line 3-30, page 14, line 4-21 and page 23, line 6-18.

In total the indicated claim and portions of the specification are directed to therapeutic agents that are polymers or are embedded in polymers. Original claim 3 recites "the therapeutic agents are selected from the group consisting of drugs, cells and polymers and diagnostic or therapeutic devices" claim 5 states that these polymers can be for example solid matrices, porous matrices, hydrogels. Page 8 teaches, "Polymers may be themselves bioactive or contain embedded or grafted bioactive molecules, peptides, lipids, drugs or other moieties." Such bioactive materials are limited to therapeutic agents. Page 12 teaches, "Polymers may be therapeutic or serve as the means for delivering therapeutic agents." The description of uses on this page are two-fold. In the first, the polymers are the therapeutic agent "Polymers may be inserted in simple spaces created via device insertion or in larger spaces created as a result of initially creating tissue defects, voids or other cavities. Voids created as a result of disease, defect or surgical procedure are filled with adhesive polymers that facilitate void cavity wall bonding and healing." Secondly, the polymers are used to deliver therapeutic agents. The first function is

expanded on page 14. The second is expanded on page 23. The two functions of polymers thus are as follows as therapeutic agents or as carriers of therapeutic agents. In describing the types of polymers to be used therapeutically, claim 5 states that the therapeutic agents of claim 3 comprise porous matrix, hydrogel, colloidal suspension, microparticle, microcapsule, nanoparticle or combination. The second function involves embedding of bioactive agents into polymers. Applicants argue that this indicates that the polymers are carriers. While the nature of the polymer as delivering bioactive agents is not in dispute, the question that arises is the disclosure of the use of "porous matrix, hydrogel, colloidal suspension, microparticle, microcapsule, nanoparticle or combinations" as delivery agents as opposed to therapeutic agents is in question. The as originally filed disclosure does not appear to contemplate use of porous matrix, hydrogel, colloidal suspension, microparticle, microcapsule, nanoparticle as carriers only as therapeutics. Therefore the limitation is impermissible NEW MATTER.

Claim interpretation

The instant specification has described the endomural zone as the middle zone of an organ, organ component or tissue structure. As guidance, applicants have described the endomural zone to correspond roughly to the central 80% of these structures. In the heart, the myocardium fits this description as evidence in the accompanying drawings in Ross (Composition of the Heart, online article June 1999). Specifically, as evidenced in the drawings depicting the layers of the heart, the endocardium and epicardium surround the myocardium. The myocardium is roughly 80% of the heart layer. In the spinal cord, the lateral corticospinal tract appears to be in the area of the spinal cord that can be considered the endomural zone as

evidenced by William et al (The Human Brain: Dissection of the Real Brain, January 1997, Chapter 1). Roughly 80% of the spinal cord is comprised of central cord, which encompasses the lateral corticospinal region.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4, 6, 7, 15-18, 20-23, 25, 28, 29, 32 and 35-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Altman (US 6,585,716 B2; see entire document). **This rejection is maintained from the office action mailed 10/4/04 and 9/7/05 and restated below.**

Altman teaches a drug delivery device for methods of treating the heart for injecting therapeutic agents into the myocardium. The method involves penetrating and entering the endomural zone (myocardium) with delivery of the agents to the endomural zone. Agents are delivered in microformulations such as microspheres (encompassing microcapsules and microparticles) as recited in claim 1. The agents are delivered using a tubular "means for delivery", which is a means of delivery similar to that disclosed in the instant specification. As well, Altman et al teach that controlled release matrices such as those made of polymers can be used to deliver the drug (see e.g. col 6, line 8-13) as recited in claims 3 and together create a bioactive polymer as recited in claim 32. Drugs used include growth factors and peptides and

angiogenesis agents (see e.g. col 5, line 48-56 and col 4, line 1) or drugs as recited in claim 3, 6, 7, 28 and 29. The delivery device has a guidance system as recited in claim 23 and a hollow penetrating element i.e. a needle attached to a catheter as recited in claim 36 and 37 (see e.g. bridging paragraph col 3-4). The instant specification teaches that the means for creating a void can be a simple catheter or needle. Therefore, the needle of Altman et al creates a void by insertion and exit from the tissue similar to that recited in claim 15 and 25 and is comprised of metal as recited in claim 16. The catheter is flexible as recited in claim 17. Drugs are stored in a reservoir attached to the catheter and pumped automatically into the lumen of the drug delivery catheter through the penetrating element into the target (see e.g. col 5, line 15-39) as recited in claim 18, 21 and 22. Furthermore, sensors can be used with the device for electrical sensing (see e.g. col 5, line 65-67) as recited in claim 20. The delivery can be percutaneously or surgically (see e.g. col 5 , line 23-28) as recited in claim 35.

Claims 1, 3, 6, 7, 15-19, 21-23, 25, 34, 36 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Altman (US 6,102,887; see entire document). **This rejection is maintained from the office action mailed 10/4/04 and 9/7/05 and restated below.**

Altman teaches a drug delivery device for methods of injecting therapeutic agents into the myocardium through a distensible penetrating element with a chamber for holding the agent (se e.g. abstract). Specifically, the device is designed to penetrate the endocardium and inject drugs deep into the myocardium (see e.g. col 3, line 9-25). Agents are delivered in microformulations such as microspheres or nanoparticles or polymers (see e.g. col 12, line 29-30) as recited in claim 1. The agents are delivered using a tubular "means for delivery", which is

a means of delivery disclosed by the instant specification. The agents are in microspheres or nanoparticles, which are locally delivered to the myocardium. Numerous agents are envisioned for delivery such as small molecules and macromolecules such as growth factors and polymers, which would fill the voids (see e.g. col 11 line 1 through 30 and figure 4a) as recited in claims 3, 6, and 7. The device comprises a penetrating end and is a hollow tube such as a needle (see e.g. col 4, line 11-12). Furthermore, an expansile cutter is included with the device. This expansile cutter is comprised of an expanding prong fixation that is sharpened to penetrate and spread the tissue (see e.g. col 9, line 22-44) as recited in claim 15, 19 and 25. The device comprises a needle and is thus comprised of metal as recited in claim 16. The drug delivery tube is comprised of a catheter and is thus flexible as recited in claim 17, 36 and 37 (see e.g. col 4, line 41-45) and is connected to reservoir (col 3, line 9-25) as recited in claim 18. Osmotic pumps or piston chambers drive drug delivery as recited in claims 21-23 (see e.g. col 6, line 40 through col 7, line 12) and is guided by a guiding catheter (see e.g. col 12, line 61-63) as recited in claim 23. The expansile cutters, create a void into which is deposited the agents for delivery (see e.g. col 10, line 48-54) as recited in claim 34.

Claims 1, 3, 6, 7, 14-16, 18, 20-24, 32 and 34-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Haim et al, (US 6,309,370 B1; see entire document). **This rejection is maintained from the office action mailed 10/4/04 and 9/7/05 and restated below.**

Haim et al teach an apparatus for intracardiac administration of growth factors into the myocardium (see e.g. abstract and col 3, line 24-42). Agents are delivered in microcapsules (see e.g. col 7, line 6-16). The agents are delivered using a catheter or tubular "means for delivery",

which is a means of delivery disclosed by the instant specification. The drugs are delivered as microcapsules as recited in claim 1. Growth factor drugs such as FGF or VEGF are envisioned for delivery (see e.g. col 9 line 4-10) as recited in claims 3, 6 and 7. The device comprises a laser beam that conveys a wave-guide to create channels into which the drugs are deposited (see e.g. col 5, line 20-21 and col 6, line 41-44) as recited in claims 14 and 34. The drug delivery device comprises a hollow needle, which is inserted into the heart with a laser beam that conveys a wave-guide to create channels or voids (see e.g. col 5, line 20-21 and col 6, line 41-44) as recited in claim 15. The device comprises a needle and is thus comprised of metal as recited in claim 16 and tubular as recited in claim 36. The device is connected to reservoir (col 13, line 1-15) as recited in claim 18 and delivered by pumps and is guided by a guiding catheter (see e.g. col 7, line 25-31) as recited in claims 21-23. A series of sensors for guidance, a position sensor and a optical sensor and one for identification of sites, a physiological sensor, a pressure sensor, an ultrasound sensor (see e.g. col 3, line through col 6, line 28) as recited in claim 20, 24. The organ can be accessed percutaneously (see e.g. col 6, line 30-59) as recited in claim 35.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altman (US 6,585,716 B2; see entire document) or Altman (US 6,102,887; see entire document) or Haim

et al, (US 6,309,370 B1; see entire document) in view of Benjamin and McMillan (Circ Res, 1998, Vol 83, pages 117-132; see entire document). **This rejection is maintained from the office action mailed 10/4/04 and 9/7/05 and restated below.**

Applicants claim a method, devices and kits for treatment comprising locally penetrating and entering the body of an organ to gain access to an endomural zone. The device deposits drugs such as heat shock proteins (HSP) into the endomural zone.

The teachings of Altman, Altman and Haim et al are described above and are applied as before except; neither Altman, Altman and Haim et al teach use of heat shock proteins.

Benjamin and McMillan teach that HSP enhances the speed of recovery of the Ischemic Heart (see e.g. page 119, col 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the drugs and growth factors taught by Altman, Altman and Haim et al with the HSPs taught by Benjamin and McMillan because Altman, Altman and Haim et al et al teach that it is within the ordinary skill of the art to deliver drugs to the myocardium to treat cardiac vascular disease and because Benjamin and McMillan teach that it is within the ordinary skill of the art to enhance recovery of an ischemic heart with administration of hsps. One would have been motivated to do so in order to receive the expected benefit of improved myocardial function, preserved metabolic functional recovery, reduction of infarct size (see e.g. page 119, col 2). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brosamle et al (The Journal of Neurosciences, 2000, Vol 20:21, pages 8061-8068; see entire document) in view of Altman (US 6,585,716 B2; see entire document) or Altman (US 6,102,887; see entire document) or Haim et al, (US 6,309,370 B1; see entire document). **This rejection is maintained from the office action mailed 10/4/04 and 9/7/05 and restated below.**

Applicants claim a method, devices and kits for treatment comprising locally penetrating and entering the body of an organ to gain access to an endomural zone. Applicants recite a use of kits comprising devices and a void filling material for nerve regeneration.

Brosamle et al teach the use of a device in which recombinant humanized IN-1 Fad antibody is delivered through by a pump through a catheter to the intrathecal space of the spinal cord. Specifically, a small hole in the dura matter was made and a catheter connected to a small osmotic pump was inserted into the subdural space close to the lesion (see e.g. figure 4). Following administration of rIN-1 Fab induced regeneration of transected spinal cord axons was induced (see e.g. page 8065, col 1, paragraph 3).

Brosamle et al do not teach that the device has an end penetrating or cutting means with which the device is inserted into the endomural zone.

The teachings of Altman, Altman and Haim et al are described above and are applied as before.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the device and methods of treatment for nerve regeneration of Brosamle et al with the device of Altman, Altman and Haim et al because Brosamle et al teach that it is within the ordinary skill of the art to administer drugs through a catheter into the subdural space

for infusion into a lesion and because Altman, Altman and Haim et al et al teach that it is within the ordinary skill of the art to use a drug delivery device that delivers drugs into the depths of the tissue. One would have been motivated to do so in order to receive the expected benefit of minimally invasive delivery of drugs in a local sustained manner for more effective drug effects (see e.g. US 6,309,370, col 2, line 50 through col 3, line 11). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 102 and 103 on pages 12-16 of the amendment filed 4/19/07. In general, applicants' argument are that the references does not teach forming a void, cavity, containment space or reservoir" by cutting or permanently removing tissue. Applicants' arguments filed 4/19/07 have been fully considered but they are not persuasive. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Absent evidence to the contrary, the needle tracks and channels as taught by Altman and Haim meet the limitations of a void or cavity as recited in the instant claims. Furthermore, that

the tissue or space refills once the needle is removed is excluded by the disclosure in the prior art of formation of channels and needle tracks.

Specifically, Altman et al (716) teach, "The catheter distal tip 24 includes a penetrating element 28, for example a curved or helical needle, which is selectively extended from the distal tip and is forced through the wall of the vein, and into the myocardium. Therapeutic agents are then injected into the myocardium through the catheter and needle." And furthermore, "To enhance the retention of the therapeutic agents in the needle track and/or within the myocardium in the face of natural fluid flow from the myocardium into the vein, the venous flow path is shut off by occluding the coronary ostium 10 with the guide catheter which has occluding mechanism 29". Hence, Altman et al absent evidence to the contrary teaches creation of a void, the needle track which is then filled with agents.

Altman et al (887) "The penetrating structure 30 is shown to be a hollow helical needle for securing the delivery catheter to prevent misplacement which may result because of the motion of the beating heart. The drug delivery sites may be in the left ventricular free wall 13, the left ventricular apex 15, or the ventricular septum 18. In other embodiments the penetrating structure could incorporate a solid helix, a hollow centrally located needle, a solid straight centrally located needle, curved needles, engagement pinchers or crossing penetrating needle structures, or appropriate combinations of these structures" (col 4, line 5-14). Inherently the design of the hollow needles leaves needle tracks as explicitly described in Altman (716). Furthermore, Altman (887) teaches use of expanding prong fixation system with prongs. "The prongs are designed to penetrate the body tissue and spread apart when the penetrating drug delivery element (the needles 865) advances axially out the distal end of the catheter body and

into the body tissue to be injected" (col 9, lines 33-37). Col 10, line 17 describes the spreading of the prongs, which inherently results in spreading of the tissues, which would create a void.

Haim teaches, "In some of these methods, known commonly as percutaneous myocardial revascularization (PMR), a catheter is inserted into the heart, and a laser beam is conveyed by a waveguide in the catheter to create channels through the endocardium into the myocardium. In others of these methods, known as transmyocardial revascularization (TMR), a probe is inserted through the chest wall and used to create channels that penetrate into a chamber of the heart through the epicardium and the myocardium" (col 6, line 40-46). Similarly to needle tracks, these channels inherently comprise voids or spaces. This is exemplified in col 7, line 6-16), "In these preferred embodiments, the growth factor drug is preferably contained in a slow-release capsule, made of an appropriate solid drug delivery medium, as described, for example, in U.S. Pat. No. 4,588,395 or 4,578,061, mentioned above. The capsule is inserted into the LMR channel or may, alternatively, be forced into the myocardium without the use of LMR."

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

Joe Woitach
AU1633